

REMARKS

The specification has been amended to correct an obvious error in equation (14) on page 34.

Claims 1-66 were pending in the application. Claims 60-65 are withdrawn from consideration as being directed to non-elected species. In the Office Action mailed on November 29, 2006, claims 1-59 and 66 are rejected. In the instant Amendment, claims 1-16, 18-47, 49, 50, 52, 53, 55, and 66 have been amended for clarity. New claims 67-70 are added. Claim 19 has been cancelled without prejudice. Upon entry of the instant Amendment, claims 1-18 and 20-70 will be pending.

Claims 1, 33, and 66 have been amended to add an additional displaying or outputting step. Support for the amendments are found, for example, at page 44, line 16, through page 46, 17; page 57, line 16 through page 59, line 32; and Figures 11 and 49 of the specification. Figure 11 provides an example of such displaying or outputting step. For example, Figure 11 illustrates an outputting step that outputs inter-slide-error corrected *trans_I*. It will be clear to one skilled in the art that outputting the profiles is not limited to outputting to linked external component(s), but may alternatively or additionally be outputting to internal component(s). It will also be clear to one skilled in the art that the claimed methods can, but need not be, computer-implemented, and that, for example, the displaying or outputting step can be done by, for example, by communicating to a person orally or in writing (e.g., in handwriting).

Claim 1 has been amended to recite “generating at least one error-corrected experiment profile of at least one of a plurality of pairs of profiles $\{A_m, C_m\}$ ” in the preamble. Claim 1 has also been amended to clarify the definitions of a plurality of pairs of profiles $\{A_m, C_m\}$, an experiment profile A_m , a reference profile C_m , experiment profiles $\{A_m\}$, reference profiles $\{C_m\}$, average reference profile \bar{C} , and a first error-adjusted experiment profile A'_m . Claim 1 has also been amended to clarify the definitions of data sets $\{\bar{C}(k)\}$ and $\{A'_m(k)\}$, which correspond to profiles \bar{C} , and A'_m , respectively. Support for the amendments may be found, for example, at page 33, line 30, through page 34, line 29; and at page 36, line 19, through page 37, line 8 of the specification.

Claim 1 has also been amended to recite experiment profile A_m and reference profile C_m as comprising a first data set (e.g., $\{A_m(k)\}$) and a second data set (e.g., $\{C_m(k)\}$),

respectively. Claim 1 has been further amended to recite both first and second data sets as comprising measurements or transformed measurements of a plurality of different cellular constituents. Support for the amendment can be found, for example, at page 34, lines 4-8 and page 36, lines 19-23 of the specification. Claim 1 has been further amended to recite k as an index of measurements or transformed measurements of a plurality of different cellular constituents. Support for this amendment can be found, for example, at page 25, lines 9-11.

Claim 1 has been further amended to recite an adjusting step (c) that generates error-corrected profile. Support for this amendment is found, for example, in the original claim 1 and at page 34, lines 27-29 of the specification.

Claims 2-5 have been amended to be consistent with the language of amended claim 1. Claim 4 has amended for clarity and to correct an error in the equation for calculating the first error-corrected profile. Support for the amendments may be found, for example, at page 33, line 30, through page 34, line 29 of the specification. Claim 5 has also been amended to recite a second error-corrected experiment profile A''_m . Support for the amendment can be found, for example, at page 35, line 19, through page 36, line 15 of the specification.

Claim 6 has been amended to be consistent with claim 5. Support for the amendment can be found, for example, at page 35, line 19, through page 36, line 15 of the specification. Claim 7 has been amended to correct a grammatical error. Claim 8 has been amended to be consistent with the language of claim 1.

Claims 9 and 10 have been amended to recite errors $\{\sigma'_m\}$ of data set $\{A'_m(k)\}$ in the first error-corrected experiment profiles A'_m . Support for the amendment can be found, for example, at page 35 lines 1-8 of the specification. Claims 9 and 10 have also been amended to be consistent with the language of claim 1.

Claims 12 and 13 have been amended to recite errors $\{\sigma''_m\}$ of data set $\{A''_m(k)\}$ in the second error-corrected experiment profile A''_m . Support for the amendment can be found, for example, at page 36, lines 16-18 of the specification. . Claim 14 has been amended to be consistent with the language of claim 1.

Claims 15, 16, and 18-20 have been amended to be consistent with the language of claim 1. Support for the amendment can be found, for example, at page 33, line 30, through page 34, line 29 of the specification.

Claim 18 has been amended to depend from claim 1 instead of 14. Support for the amendment can be found, for example, at page 34, lines 4-8 and page 36, lines 19-23 of the

specification. Claims 18 and 19 have also been amended to recite transformed data sets $\{TA_m(k)\}$ and $\{TC_m(k)\}$ as first and second data sets that correspond to experiment profile A_m and reference profile C_m , respectively. Support for the amendment can be found, for example, at page 36, lines 19-23; and in section 5.4 of the specification, at page 48, line 9, through page 57, line 14, in particular, at page 54, lines 5-10 of the specification.

The original claim 19 has been cancelled. A new claim 19 replaces the original claim 19 due to the difficulty in illustrating changes in the equations. The new claim 19 has replaced $A_m(k)$ in favor of $TA_m(k)$, in order to be consistent with the language of claim 18. The new claim 19 has also been amended to add a missing bracket in both equations. Support for the amendment is found, for example, in equation (61) at page 54, where the variable x in equation (61) is replaced by $XA_m(k)$ or $XC_m(k)$, respectively to render the equations in claim 19.

Claim 20 has been amended to depend from claim 1 instead of claim 14 and to be consistent with the language of claim 1. Claim 20 has also been amended to recite a positive method step (a0) of removing nonlinearity from measurements or transformed measurements of a plurality of different cellular constituents. Claim 21 has been amended to recite a more detailed removing step and to be consistent with the language of claim 20. Support for the amendments can be found, for example, at page 34, lines 4-8; page 38, line 8, through page 39, line 21; and Figure 11 of the specification.

Claims 22 and 23 have been amended to be consistent with the language of claim 21 and to clarify a subset of measurements as a first subset and a second subset. The first subset comprises measurements or transformed measurements between an experiment profile and an average profile. The second subset comprises measurements or transformed measurements between a reference profile and an average profile. Support for the amendment can be found, for example, at page 38, lines 16-22; page 8, line 17, through page 9 line 13; and page 13, line 15, through page 14, line 9 of the specification.

Claim 23 has been amended for clarity to recite that measurements or transformed measurements of a plurality of different cellular constituents may be ranked between an experiment profile and an average profile, or between a reference profile and an average profile. Claim 24 has been amended to be consistent with the languages of claims 1, and 20-23, from which claim 24 depends. Support for the amendment can be found, for example, at page 38, lines 16-22; page 41, lines 20-26; and Figure 3 of the specification.

Claim 25 has been amended to depend from claim 1. Claim 1 has also been amended to recite a positive method step (a0) for normalizing an experiment profile or a reference profile. Claims 26-28 has been amended to be consistent with the language of claims 1 and 25. Support for the amendments is found, for example, at page 36, line 24 through page 37, line 23 of the specification.

Claim 29 has been amended to clarify how specific embodiments of averages $\overline{A_m}$ and $\overline{C_m}$ are calculated, *e.g.*, by excluding the highest 10% of the measurements or transformed measurements in the corresponding data sets. Support for the amendment can be found at page 38, lines 1-8, particularly lines 6-7 of the specification. Claim 29 has also been amended to remove redundant information that has already been recited in claim 26.

Claim 30 has been amended for clarity similarly as claim 1. Support for the amendments is found, for example, at page 38, line 8, through page 48, line 8; section 5.4; and Figure 2 of the specification. Claims 31-34 have been amended to be consistent with the language of claims 30. The equations in claim 32 have also been amended to remove errors. Support for the amendments is found, for example, at page 36, line 24 through page 37, line 23, of the specification.

Claims 26-28, 33, 34 have been amended to correct grammatical errors.

Claim 35 has been amended to how specific embodiments of averages $\overline{XA_m}$ and $\overline{XC_m}$ are calculated, *e.g.*, by excluding the highest 10% of the measurements in the corresponding data sets. Support for the amendment can be found at page 38, lines 1-8, particularly lines 6-7 of the specification. Claim 35 has also been amended to remove redundant information that has already been recited in claim 32.

Claim 36 has been amended to recite “transforming said normalized data sets $\{NA_m(k)\}$ and $\{NA_m(k)\}$ to obtain transformed data sets $\{TA_m(k)\}$ and $\{TA_m(k)\}$, respectively.” The amended claim 36 is consistent with the language of the amended claims 30 and 32. Claim 37 has been amended to remove redundancy that has been recited in new claim 30 and to be consistent with the language of claims 31-36. Support for the amendments is found, for example, in section 5.4 and particularly at page 54, equation (61) of the specification.

Claim 38 has been amended to be consistent with the language of claim 30. Claim 39 has been amended to remove “determining” in favor of “calculating” and to remove “using”

in favor of “based on.” Claim 39 has been further amended to recite a first difference between the transformed experiment profile and the average profile and a second difference between the transformed reference profile and the average profile. Support for the amendments can be found, for example, in the originally filed claim 21, and at page 41, lines 8, through page 42, line 16 of the specification. Claim 40 has been amended to recite a first subset of transformed measurements (between a transformed experiment profile and an average transformed profile) and a second subset of transformed measurements (between a reference experiment profile and an average transformed profile). Support for the amendment can be found, for example, at page 41, lines 20-26 of the specification. Claims 40-42 have been amended to be consistent with the language of claims 38 and 39. Additional support for the preceding amendments can be found, for example, at page 13, line 15 through page 16, line 15; page 38, line 8, through page 39, line 21; page 34, lines 4-8, and Figure 11 of the specification.

Claim 43 has been amended to be consistent with the language of claim 30. Claim 44 has amended for clarity and to correct an error in the equation for calculating the first error-corrected profile. Support for the amendments may be found, for example, at page 33, line 30, through page 34, line 29 of the specification. Claim 45 has also been amended to recite a second error-corrected experiment profile A''_m . Claims 43 and 45 have also been amended to recite processed experiment profile and processed reference profile as well as each process profile pair $\{A_m, C_m\}$. Support for the amendment can be found, for example, at page 35, line 19, through page 36, line 15 of the specification and at claim 30.

Claim 47 has been amended to correct a grammatical error. Claims 49 and 50 have been amended to be consistent with the language of claim 30. Claims 52 and 52 have been amended to be consistent with the language of claim 46 and 50, respectively. Claims 55 and 57 have been amended to be consistent with the language of claim 30.

A new claim 67 is added to replace the canceled claim 19. Claims 68 and 69 are added. Support for the new claim 67 is found, for example, at page 40, line 7, through page 57, line 14 of the specification and Figure 2. Support for claims 68 and 69 is found, for example, in the original claims 19, 58, and 59. Support for new claim 70 is found, for example, at page 40 line 7, through page 57, line 14 of the specification and Figure 2.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE REJECTIONS UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

Claims 1-57 and 66 are rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter. The Examiner contends that “[t]o satisfy 101 requirements, the claim must be for a practical application, which can be met if the claimed invention ‘transforms’ an article or physical object to a different state or thing OR the claimed invention otherwise produces a useful, concrete, and tangible result” (Office Action at page 3, second paragraph). Applicant respectfully disagrees.

While not acquiescing in the Examiner’s rejection, Applicant has amended claims 1, 30, and 66 in order to expedite prosecution. Claims 1, 30, and 66 have been amended to include an outputting or displaying step. As such, the 35 U.S.C. § 101 rejection of claims 1, 30, and 66 has been overcome in light of the amendments. Claims 2-29 depend from claim 1. Claims 31-57 depend from claim 30. Therefore, the rejection 35 U.S.C. § 101 of claims 2-29 and 31-57 has also been overcome.

Accordingly, Applicant respectfully requests that the 35 U.S.C. § 101 rejection of claims 1-57 and 66 be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 112 SHOULD BE WITHDRAWN

Claims 1-59 and 66 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses the rejections as follows.

THE 35 U.S.C. § 112 REJECTION OF CLAIMS 1-59 AND 66 SHOULD BE WITHDRAWN

The Examiner contends that claims 1-59 and 66 are indefinite because claims 1, 30, and 66 recite in the preamble “correcting errors in ... pairs of profiles.” The Examiner contends that the claim steps recite only generating an error-adjusted experimental profile A'_m , and therefore it is not clear whether an error is intended to be corrected in an experimental profile using a reference profile for each pair $\{A_m, C_m\}$ or some error generated by each pair $\{A_m, C_m\}$, is intended to be corrected for all pairs. The Examiner also contends that it is unclear whether the limitation “thereby correcting” is intended to be an active, positive method step or merely an intended result of the method. The Examiner further

contends that the relationship of the preamble and the method steps is also unclear because the preamble recites “[a] method for *correcting* . . . pairs of profiles” and the method only recites steps of calculating, determining, and generating an error-adjusted experiment profile (Office Action, third paragraph, page 4).

While not acquiescing in the Examiner’s contention, Applicant has amended claim 1, 30 and 66 for clarity in order to expedite prosecution. The amended claims 1, 30, and 66 recite an adjusting step (c) where errors in an experiment profile A_m are corrected based on a differential reference profile determined previously in step (b). The method recites steps of calculating, determining and adjusting. Applicant also has removed the “thereby” clause for further clarity. The preamble of amended claim 1 recites “a method for generating at least one error-corrected experiment profile of at least one experiment profile in a plurality of pairs of profiles $\{A_m, C_m\}$.” Step (c) of the amended claim 1 recites “to generate a first error-corrected experiment profile A'_m ,” *i.e.*, the first error-corrected experiment profile A'_m is generated as the intended result of the method. The amended language of step (c) is consistent with the language of the preamble: “a method for **generating** at least one error-corrected experiment profile.” Claims 30 and 66 have been amended similarly. Thus, the Examiner’s rejection based on the unclear relationship of the preamble and the method steps has also been obviated, and the 35 U.S.C. § 112 rejection of claims 1, 30, and 66 has been overcome in light of the amendments. Claims 2-29 depend from claim 1. Claims 31-59 depends from claim 30. Therefore, the rejection 35 U.S.C. § 112 of claims 2-29 and 31-57 also has been overcome.

The Examiner also contends that claims 1-59 and 66 are indefinite because a differential reference profile, as recited in claims 1, 30, and 66, is not clear (Office Action, fourth paragraph, page 4). Without acquiescing in the Examiner’s contention, Applicant has amended claims 1, 30 and 66 for clarity in order to expedite prosecution. The amended claims 1, 30 and 66 recite that a differential reference profile is determined based on a reference profile C_m and the average reference profile \overline{C} . See for example, at page 24, line 32, through page 25, line 6 of the specification where an error profile consisting of systematic cross-experiment errors (*e.g.*, a differential reference profile as recited in claims 1, 30 and 66) is determined by comparing the reference channel profile (*e.g.*, reference profile C_m) in the multi-channel profile with the average reference profile (*e.g.*, average reference profile \overline{C}). As such, the differential reference profile is clear. Therefore, the 35 U.S.C. § 112 rejection of claims 1, 30, and 66 has been obviated. Claims 2-29 depend from claim 1. Claims 31-59

depends from claim 30. Therefore, this 35 U.S.C. § 112 rejection of claims 2-29 and 31-59 also has been obviated.

Regarding claims 1, 30, and 66, step (c), the Examiner contends that it is not clear whether Applicant intended to limit the method steps or the data by reciting a method by which data (adjusted profiles) are generated. (Office Action, first paragraph, page 5).

Applicant has amended claims 1, 30 and 66 to recite a positive method step of adjusting experiment profile A_m to generate an error-corrected profile A'_m . In addition, Applicant has amended claims 1, 30 and 66 to replace “using” with “based on.” As such, the amended claims 1, 30 and 66 recite an active, positive adjusting method step. Thus the 35 U.S.C. § 112 rejection of claims 1, 30, and 66 has been obviated. Claims 2-29 depend from claim 1. Claims 31-59 depends from claim 30. Therefore, this 35 U.S.C. § 112 rejection of claims 2-29 and 31-59 has been obviated.

Regarding the recitation of claims 1, 30, and 66 that “constituents ... measured in a sample having subjected to condition A_m , and . . . condition C,” the Examiner contends that earlier the claims recite that A_m , and C stand for an experimental profile and a reference profile, respectively, not for “conditions” (Office Action, second paragraph, page 5), and that therefore the claims are unclear. In response, Applicant has amended claims 1, 30 and 66 to replace “condition A_m ” and “condition C” with “a first condition” and “second condition,” respectively. The 35 U.S.C. § 112 rejection based on the unclear limitation of “condition A_m ” and “condition C” thus has been rendered moot in light of the amendments to claims 1, 30 and 66, and should be withdrawn. Claims 2-29 ultimately depend from claim 1. Claims 31-59 ultimately depend from claim 30. Therefore, the 35 U.S.C. § 112 rejection of 2-29 and 31-59 also should be withdrawn.

Regarding the recitation of claims 1, 30, and 66 that a data set $\{A_m, (k)\}$ comprises measurements of a plurality of different cellular constituents measured in a sample, wherein $k = 1 \dots N$, and N is an index of measurements of cellular constituents, the Examiner contends that it is not clear whether “k” stands for kth constituent (*e.g.*, gene 5) or for a number of repetitions of measuring cellular constituents (*e.g.*, expression of genes 1-100 is measured “k” times for better statistics) (Office Action, third paragraph, page 5).

Applicant respectfully points out that amended claims 1, 30, and 66 recite that “k is an index of the number of measurements or transformed measurements of a plurality of cellular constituents, N being the total number of measurements or transformed measurements.” For

example, N is the total number of probes used and k is an index of a particular probe. See for example, page 25 lines 9-11 of the specification. As such, the term “k” is clear. Thus the 35 U.S.C. § 112 rejection of claims 1, 30, and 66 should be withdrawn. Claims 2-29 each ultimately depends from claim 1, and claims 31-59 depend from claim 30. Therefore, the rejection of claims 2-29 and 31-59 also should be withdrawn.

The Examiner contends that claims 3-14, 18-29 and 43-59 are indefinite, because claims 3 and 43 recite the limitation “wherein experimental profile and reference profile are measured in the same experimental reaction.” The Examiner contends that it is not clear whether “measuring” is intended to limit the method or data (Office Action, fourth paragraph, page 5).

Applicant has amended claims 3 and 43 for clarity to recite that “wherein said experiment profile A_m and reference profile C_m *comprise measurements or transformed measurements of cellular constituents from the same experimental reaction.*” See, for example, at page 26, lines 14-22 of the specification where such is discussed. Thus the rejection of claims 3 and 43 is obviated. Claims 4-14 and 18-29 depend from claim 3 while claims 44-59 depend from claim 43. Therefore, the rejection of claims 4-14, 18-29, and 44-59 is also obviated in light of the amendments.

The Examiner contends that claims 15, 16, and 55-59 are indefinite because claims 15 and 55 recite the limitation “wherein ... profiles ... [are] measured in a two channel microarray experiments.” The Examiner contends that claims 15 and 55 are indefinite because it is not clear whether Applicant “intended to limit the method steps OR the data by reciting a method by which data (profiles) are measured” (Office Action, first paragraph, page 6). Applicant respectfully disagrees.

The recitation that the profiles are measured in a two-channel microarray experiment further limits the data contained in the profiles since data from a single channel microarray experiment is excluded. As such, each pair of profiles A_m and C_m as recited in claims 15 and 55 only comprise data from one specific type of microarray experiment: a two-channel microarray experiment. Thus the limitations of claims 15 and 55 are clear, and the rejection of claims 15 and 55 should be withdrawn. Claim 16 depends from claim 15 and claims 56-59 depend from claim 55; therefore, the rejection of claims 16 and 56-59 also should be withdrawn.

The Examiner contends that claims 16 and 56-59 are unclear. Claim 16 recites the limitation “wherein said reference profiles ... are measured with samples labeled with a same label.” The Examiner contends that “it is not clear whether a reference profile is measured in a labeled sample, both a reference and an experimental profile are measured in two samples that are labeled with the same label, different reference profiles are measured in different samples labeled with the same label, *etc.*” (Office Action, second paragraph, page 6). Applicant respectfully disagrees.

Claim 16 expressly recites that “*said reference profiles* ... are measured with samples labeled with a same label” (emphasis added). Thus, claim 16 specifies that different reference profiles are measured in different samples labeled with the same label. Therefore, the Examiner’s contention that claim 16 is unclear for the reasons given is inconsistent with the express language of claim 16. As such, the limitation of claim 16 is clear and applies to “different reference profiles are measured in different samples labeled with the same label.” Claim 56 recites the same language in relevant part as claim 16, and thus is also clear. Claim 57 depends from claim 56. Claim 58 and 59 depend from both claims 16 and 56; therefore, they also are clear. Therefore the rejection of claims 16 and 56-59 should be withdrawn.

The Examiner contends that claims 18, 58 and 59 are indefinite, since claim 18 recites “transformed profiles comprising transformed measurements.” The Examiner contends that it is not clear what “transformation” of profiles is intended and that neither the specification nor the claims defines the transformation (Office Action, third paragraph, page 6). Applicant respectfully disagrees.

Applicant has amended claim 18 for clarity to recite “ $\{A_m, C_m\}$ are transformed profiles each comprising transformed measurements of said plurality of different cellular constituents in data set $\{TA_m(k)\}$ and data set $\{TC_m(k)\}$.” As made clear by the specification, transformation of profiles refers to mathematical transformation of the measurements of cellular constituents. Data transformation is done because “[m]easured data obtained in a microarray experiment often contain errors due both to the inherent stochastic nature of gene expression and to measurement errors from various external sources” (see, at page 48 lines 11-13 of the specification). The many sources of measurement errors that may occur in a measured signal include those that fall into three categories - additive error, multiplicative error, and Poisson error sources (see, at page 48 lines 13-15 of the specification). For example, in Section 5.4.1.2 of the specification, entitled “Intensity

Transformation,” starting at page 51, microarray intensity measurements are transformed to reduce measurement errors: “There are different measurement errors (or variances) in different intensities. The intensity error is a function of intensity itself. To overcome this problem, a function $f(x)$ is needed to transform measured data, *e.g.*, the intensity data, x to a new domain y in which the variance becomes a constant” (see page 51, lines 25 through 27, of the specification). Additional examples of transformation methods or transformed data sets are found in Section 5.4 of the specification on pages 48 through 57. As such, the specification has made clear what transformation is. Therefore, the rejection of claim 18 should be withdrawn. Claims 58 and 59 depend from claim 18, and thus the rejection of claims 58 and 59 also should be withdrawn.

The Examiner contends that claims 19, 58, and 59 are indefinite since claim 19 recites the limitation “wherein said transformed measurements are obtained according to equations.” The Examiner contends that it is not clear whether “measurements” are obtained using the recited equations or earlier obtained measurements are transformed by applying the recited equations (Office Action, fourth paragraph, page 6). Applicant respectfully disagrees.

Claim 19 has been replaced by new claim 67 due to the difficulty in indicating amendments to the equations therein. Claim 67 recites “further comprising obtaining said transformed measurements of said $\{TA_m(k)\}$ and said $\{TC_m(k)\}$ according to equations.” The language of the claim, as interpreted in light of the section of the specification discussed above in connection with claim 18, makes it clear that the equation is used to transform existing measurements. Thus, the rejection of claims 19, 58 and 59 should be withdrawn.

The Examiner contends that claims 19, 58, and 59 are indefinite, because claim 19 recites the limitation “transformed measurements ... $A_m(k)$ ” and “an experimental profile XA_m , and ... measured data set $\{XA_m(k)\}$.” The Examiner contends that claim 19 depends from claim 1 which recites $A_m(k)$ being a data set of an experimental profile, not transformed measurements. In addition, the Examiner contends that claim 1 also recites that A_m stands for an experimental profile, not XA_m , and $\{A_m(k)\}$ stands for a data set of the experimental profile, not $\{XA_m(k)\}$ (Office Action, first paragraph, page 7). Claim 19 has been replaced by new claim 67 due to the difficulty in indicating amendments to the equations therein. In new claim 67, $\{XA_m(k)\}$ and XA_m have been replaced with $\{A_m(k)\}$ and A_m , respectively. With this amendment, the experiment profiles and data sets as recited in claim 19 are consistent with the language of claim 1. Therefore, claim 19 is clearly defined and the

rejection should be withdrawn. Claims 58 and 59 depend from claim 19 and thus also are clear. Therefore, the rejection of claims 58 and 59 also should be withdrawn.

The Examiner contends that claims 20-24 and 38-59 are indefinite, since claims 20-24, 38, and 39 recite the limitation “measurements from which nonlinearity is removed.” The Examiner contends that the limitation “nonlinearity” which is removed from “measurement” is not clear. The Examiner further contends that neither the specification nor the claims define the limitation (Office Action, second paragraph, page 7). Applicant respectfully disagrees.

As the specification explains, the experiment and reference profiles $\{A_m, C_m\}$ can also be processed profiles in which nonlinearity is removed from raw or transformed experiment and reference profiles (see page 38, lines 8-9 of the specification). Methods for nonlinearity removal are also called “detrending.” In detrending, the measurement value, e.g., intensity, dependant non-linearity in all channels is minimized (see page 38, lines 10-11 of the specification). The specification further provides multiple detailed exemplary embodiments of methods of nonlinearity removal/detrending; see, for example, pages 38 through 42 of the specification. For example, a *nonlinear_diff* function, a piecewise linear curve, may be constructed as depicted in Figure 3 and at page 42 lines 8-16 of the specification. Equation (36) on page 42 further illustrates a specific method for removing nonlinearity from measurements by defining a *nonlinear_diff* function. Thus, nonlinearity removal is made clear by the disclosure in the specification, and therefore claims 20-21 and 38-39 are clear. Claims 22-24 and 40-59 depend from claim 20 and 38, respectively. Therefore, claims 22-24 and 40-59 are also clear. Accordingly, the rejection of claims 20-24 and 38-59 should be withdrawn.

The Examiner contends that claims 21-24 and 58- 59 are indefinite, because claim 21 recites the limitation “wherein said measurements from which nonlinearity is removed are obtained by a method comprising [steps] (i) . . . and (ii).” Claim 21 depends from claim 1. The Examiner contends that “[i]t is not clear whether steps (i) and (ii) [of claims 21] are intended to be active, positive method steps of the method recited in claim 1 or merely an intended use/result of the method” (Office Action, third paragraph, page 7). Applicant respectfully disagrees.

Claim 21 has been amended to make it clear that the steps recited therein are positive method steps. Claim 21 as amended recites a two-step method, with a determining step (a0i)

and an adjusting step (a0ii), for removing nonlinearity in measurements or transformed measurements of a plurality of cellular constituents before step (a) of claim 1 is performed.

Claim 21 depends from claim 1. The Examiner further contends that then “it is not clear where steps (i) and (ii) fit within the method of claim 1, *i.e.*, whether steps (i)-(ii) are additional steps or they are intended to substitute steps recited in claim 1” (Office Action, third paragraph, page 7). Applicant respectfully disagrees.

As discussed above, claim 21 depends from claim 20, which specifies that the removing of nonlinearity is prior to said calculating step (a) (of claim 1). Thus the method of removing specified in claim 21 comprises additional steps done prior to the calculating step of claim 1. Therefore, the Examiner’s contention that the intended limitation in claim 21 is not clear is erroneous, and the rejection of claim 21 should be withdrawn. Claim 22-24 and 58-59 depend from claim 21, and the rejection of claims 21-24 and 58-59 also should be withdrawn.

The Examiner contends that claims 21-24 and 58-59 are indefinite, because claim 21 recites determining an average profile of all experiment A_m , and reference profiles C_m . The Examiner contends that the meaning of the average profile is not clear (Office Action, fourth paragraph, page 7). Applicant respectfully disagrees.

Step (i) in claim 21 recites “determining **an** average profile of first experiment profiles and first reference profiles.” It is clear that there is only **one** overall average profile determined based on the first experiment profiles and the first reference profiles together. A description of the average profile is found, for example, at page 38, lines 11 through 15 and page 41, lines 14-19 of the specification. As such, the meaning of the average profile is clear. Therefore, claim 21 is clear. Claims 22-24 and 58-59 depend from claim 21 and therefore are also clear. Thus, the rejection of 21-24 and 58-59 should be withdrawn.

The Examiner contends that claims 21-24 and 58-59 are indefinite, because claim 21 further recites the limitation of “adjusting each A, or C, based on a difference between said A_m or C_m and said average profile.” The Examiner contends that the antecedent basis of the limitation “said average profile” is not clear because step (i) recites both experimental and reference average profiles. The Examiner further contends that criteria, steps, or algorithms of “adjusting” are also unclear (Office Action, first paragraph, page 8). Applicant respectfully disagrees.

As discussed above, the average profile is clearly defined and thus the Examiner's rejection based on an unclear meaning of "said average profile" is obviated. Applicant has amended claim 21 to recite adjusting based on a first difference between said first experiment profile and said average profile, or based on a second difference between said first reference profile and said average profile. As such, the first difference is determined between said first experiment profile and said average profile. The second difference is determined between said first reference profile and said average profile. Description of "the first or second difference" is found, for example, at page 38, lines 11-15 of the specification. As such, the difference used to adjust each first experiment profile or first reference profile is clearly defined. In addition, an exemplary adjusting process is illustrated, for example, at page 38, line 30, through page 39, line 9, in particular in the equations (30) and (31) of the specification. Thus, the adjusting step also is clearly defined. The rejection of claim 21 also is obviated. Claims 22-24 and 58-59 depend from claim 21. Therefore, the rejection of claims 21-24 and 58-59 should be withdrawn.

The Examiner contends that claims 22-24 and 58-59 are indefinite, because claim 22 recites the limitation "wherein said difference is determined using a subset of measurements in the profiles." The Examiner contends that the antecedent basis of the limitation "the profiles" is not clear because claim 21, from which claim 22 depends, recites different types of profiles. The Examiner also contends that it is also not clear whether "determining" is intended to be an active, positive method step or merely an 'intended use of the method (Office Action, second paragraph, page 8).

Applicant has amended claim 22 for clarity. The amended claim 22 recites a positive calculating step as a method step, and specifies "a first subset of said measurements or transformed measurements of said plurality of different cellular constituents in said first experiment profile and said average profile ... and ... a second subset of said measurements or transformed measurements of said plurality of different cellular constituents in said first reference profile and said average profile." As such, the rejection of claim 22 is obviated. Claims 23, 24, 58 and 59 each depends from claim 22. Therefore, claims 22-24 and 58-59 should be withdrawn.

The Examiner contends that claims 23, 24, 58, 59 are indefinite, since claim 23 recites the limitation "wherein said subset of measurements in the profiles consists of measurements that are ranked similarly between an experiment or reference profiles and said average

profile.” The Examiner contends that it is not clear whether the limitation “the profiles” is intended to comprise an average profile, only A_m , or C_m , both A_m , and C_m , *etc.* The Examiner also contends that it is not clear what is ranked, *e.g.*, experimental measurements, reference measurements, average measurements, *etc.*, and between what ranked measurements the similarity is assessed. The Examiner further contends that it is also unclear whether measurements are ranked, for example, in each profile, or measurements are ranked between the value of measurements in a reference profile (*e.g.*, maximum measurement is 10) and the value of measurements in an average profile (*e.g.*, minimum measurement is 5) (*i.e.*, experimental measurements are ranked between 5 and 10) (office Action, third paragraph, page 8).

Applicant has amended claim 23 to recite “measurements or transformed measurements of said plurality of different cellular constituents that are ranked similarly between said first experiment profile and said average profile” and to recite “measurements or transformed measurements of said plurality of different cellular constituents that are ranked similarly between said first reference profile and said average profile.” As such, the amended claim 23 is clear. As such, the rejection of claim 23 is obviated. Claims 24, 58 and 59 depend from claim 23. Therefore, the rejection of claims 23, 24, 58 and 59 should be withdrawn.

The Examiner contends that claims 24, 58 and 59 are indefinite, because claim 24 recites the limitation “said comparing in step (ii) is carried out by a method comprising [steps] (ii1) binning measurements ... and (ii4).” The Examiner contends that the limitation “said comparing” does not have an antecedent basis because claim 23 does not recite a step of “comparing.” The Examiner also contends that it is further unclear whether each bin comprises only A or C measurements or both A_m and C_m (Office Action, first paragraph, page 9).

Applicant has amended claim 24 to replace “said comparing in said step (ii)” with “said removing step (a0ii),” which has proper antecedent basis. Applicant also has amended claim 24 to recite “binning said first subset into a first plurality of bins, wherein each of said first plurality of bins consists of measurements or transformed measurements of said plurality of different cellular constituents in said first experiment profile and said average profile having a value in a given range,” and to recite “binning said second subset into a second plurality of bins, wherein each of said second plurality of bins consists of measurements or

transformed measurements of said plurality of different cellular constituents in said first reference profile and said first average profile having a value in a given range.” As such, the respective bins of claim 24 comprise *either* measurements or transformed measurements of said plurality of different cellular constituents in said first experiment profile and said average profile *or* measurements or transformed measurements of said plurality of different cellular constituents in said first reference profile and said average profile. Thus, the rejection of claim 24 is obviated in light of the amendments, and should be withdrawn. Claims 58 and 59 depend from claim 24. Therefore, the rejection of claims 24, 58 and 59 should be withdrawn.

Claim 24 depends indirectly from claim 1. The Examiner contends that “[i]t is unclear whether steps (ii1)-(ii4) recited in claim 24 are intended to be active, positive steps of the method recited in claim 1 or merely an intended use of the method.” The Examiner further contends that “it is not clear where the steps fit within the steps recited in claim 1 and whether the steps (ii1)-(ii4) are intended to be added to or substitute for steps of claim 1. As the intended limitation is not clear, claims 24 and 58-59 are indefinite” (Office Action, second paragraph, page 9). Applicant respectfully disagrees.

Claim 24 depends indirectly from claim 20, which has been amended to recite an affirmative step of removing nonlinearity, prior to said calculating step (a) of claim 1. Claim 21, which also depends from claim 20, further specifies the affirmative removing method step. Claim 21 recites a determining step (a0i) and an removing step a0(ii), for removing nonlinearity in measurements of a plurality of cellular constituents in producing an experiment profile A_m or reference profile C_m . Claim 24 depends from claim 21 and further specifies the removing step (a0ii) of claim 21. Therefore, claim 24 recites active and positive steps that further limit the method of claim 1. As such, claim 24 is clear. Thus, rejection of claim 24 should be withdrawn. Claims 58 and 59 depend from claim 24, and therefore the rejection of claims 58 and 59 also should be withdrawn.

The Examiner contends that claims 26 and 58-59 are indefinite, because claim 26 recites the limitation “wherein normalized profile . . . is obtained by a method comprising normalizing . . . according to equation.” Claim 26 depends from claims 1-14 and 25. The Examiner contends that “[i]t is not clear whether ‘obtaining a normalized profile’ is intended to be an active positive method step of the method recited in the claims 1-14 and 25 or merely an intended use of the method and where the step of normalizing fits within the method

recited in claims 1-14, 25.[sic] As the intended limitation is not clear, claims 24[6] and 58-59 are indefinite” (Office Action, fourth paragraph, page 9). Applicant respectfully disagrees.

Applicant has amended claim 26 to recite an active positive normalizing step, which further limits the normalizing step of claim 26. Claim 26 depends from claim 25, which has been amended to recite an active positive normalizing step (a0) that occurs prior to the calculating step (a) (of claim 1). The rejection is thus obviated and should be withdrawn. Claims 58 and 59 depend from claim 26 and therefore the rejection of claims 58 and 59 also should be withdrawn.

The Examiner contends that claims 30-59 are indefinite, because claim 30 recites a step of “processing profiles.” The Examiner contends that it is not clear what specific steps, algorithms, or methods of “processing” are intended. Thus the Examiner contends that claims 30-59 are indefinite (Office Action, fifth paragraph, page 9). Applicant respectfully disagrees.

Claim 30 as amended recites a step (a) of processing experiment profile XA_m and reference profile XC_m to produce experiment profile A_m and reference profile C_m , respectively. Figure 2 provides an exemplary embodiment of processing, which includes by way of example normalization, transformation and detrending (i.e., removal of nonlinearity). More detailed description can be found, for example, at page 40, line 7, through page 57, line 14 of the specification; including an entire section on transformation (see Section 5.4). As such, “processing” as recited in claim 30 is clear. Thus, the rejection of claim 30 should be withdrawn. Claims 31-59 depend from claim 30; and therefore, the rejection of claims 31-59 also should be withdrawn.

The Examiner contends that “[c]laim 30 recites an experimental profile XA_m in the preamble and after step (c) and a processed profile A_m in step (a). However, in step (d) the claim recites “said experimental profile A_m .” The Examiner further contends that “[i]t is not clear whether XA_m or A_m is intended to be ‘an experimental profile and what profile is used in step (d) for generating an error-adjusted experimental profile A'_m ” (Office Action, first paragraph, page 10). Applicant respectfully disagrees.

Applicant has amended claim 30 to recite “an experiment profile XA_m ” in the preamble and “a processed experiment profile A_m ” in step (d). As such, the amendments render the Examiner’s rejection moot. Thus, claim 30 is clear.

The Examiner states that claim 30 also recites XC_m being a reference profile and C_m being a processed reference profile in the preamble and in step (a), and that C_m stands for a reference profile in step (b). The Examiner further contends that it is not clear whether XC_m or C_m is intended to be a reference profile. According to the Examiner, the relationship of an experiment profile XC_m , a processed profile A_m , a reference profile XC_m , and a reference processed profile C_m is not clear. Thus, the Examiner contends that claims 30-59 are indefinite (Office Action, second paragraph, page 10). Applicant respectfully disagrees.

Applicant has amended claim 30 to recite “a reference profile XC_m ” in the preamble and “processed reference profiles $\{C_m\}$ ” in step (b). As such, the amendments render the Examiner’s rejection moot. Thus, claim 30 is clear.

Claim 30 recites in step (a) “to obtain a plurality of ... processed profiles.” The Examiner further contends that it is not clear whether “obtaining” is intended to be an active, positive step of the method or merely an intended result. As the intended limitation is not clear, claims 30-59 are indefinite (Office Action, fourth paragraph, page 10). Applicant respectfully disagrees.

Claim 30 recites “processing said plurality of pairs of profiles $\{XA_m, XC_m\}$ to obtain a plurality of pairs of processed profiles.” It is apparent that obtaining a plurality of pairs of processed profiles is an inevitable result of the step of processing said plurality of pairs of profiles $\{XA_m, XC_m\}$. As such, claim 30 step (a) as claimed is clear and thus the rejection of claim 30 should be withdrawn. Claims 31-59 depend from claim 30; therefore the rejection of claims 31-59 also should be withdrawn.

The Examiner contends that claims 36-59 are indefinite, because claim 36 recites the limitation “transforming normalized profiles to obtain transformed profiles.” The Examiner contends that it is not clear what particular steps or algorithms of “transformation” are intended and to what (*e.g.*, profiles, different data set, graphs, *etc.*) profiles are transformed (Office Action, fifth paragraph, page 10). Applicant respectfully disagrees.

As discussed above regarding the rejection of claim 18, transformation and particular steps or algorithms of transformation are disclosed in Section 5.4 of the specification at pages 48-57, so as to render the term transformation clear. Claim 36 has been amended to recite “transforming said normalized data sets $\{NA_m(k)\}$ and $\{NA_m(k)\}$ to obtain transformed data sets $\{TA_m(k)\}$ and $\{TA_m(k)\}$, respectively.” As such, claim 36 is clear; thus the rejection of

claim 36 should be withdrawn. Claims 37-59 depend from claim 36. Therefore, the rejection of claims 36-39 should be withdrawn.

The Examiner contends that claims 37-59 are indefinite, because claim 37 recites the limitations $TA_m(k)$ and $TC_m(k)$, which the Examiner contends are undefined (Office Action, first paragraph, page 11). Applicant respectfully disagrees.

Applicant respectfully points out that $TA_m(k)$ is defined in claim 36 as amended by the following language: “a transformed data set $\{TA_m(k)\}$, where said transformed data set $\{TA_m(k)\}$ is said first data set of said processed experiment profile A_m when further processing of said data set $\{TA_m(k)\}$ does not occur.” Applicant also respectfully points out that $TC_m(k)$ is defined in claim 36 as amended by the following language: “a transformed data set $\{TC_m(k)\}$, where said transformed data set $\{TC_m(k)\}$ is said second data set of said processed reference profile C_m , when further processing of said data set $\{TC_m(k)\}$ does not occur.” Claim 37 depends on claim 36. As such, the rejection of claims 37 is moot in light of the amendments. Claims 38-59 depend from claim 37. Therefore, the rejection of claims 37-59 should be withdrawn.

The Examiner contends that claims 39-59 are indefinite, because claim 39 recites the limitation “wherein removing . . . is carried out by a method comprising [steps] (a1) and (a2).” The Examiner contends that it is not clear whether applicants intended to limit the method steps OR the data. If the latter, then the Examiner contends that it is not clear what further limitation of data used in the claimed method is intended by the methods of obtaining the data. If the former, then the Examiner contends that claims should be rewritten to clearly delineate the method steps (Office Action, second paragraph, page 11). Applicant respectfully disagrees.

Applicant respectfully points out that claim 39 depends from claim 38, which depends indirectly from claim 30. Claim 30 recites an affirmative processing step (a), while claim 38 further specifies that the processing step (a) comprises a step of removing nonlinearity. Claim 39 further delineates the method of removing nonlinearity by reciting steps (a1) and (a2). As such, claim 39 as amended comprises clearly delineates method steps (i) and (ii) which are parts of the processing step (a); therefore claim 39 is clear. Because claims 40-59 depend from claim 39, they also are clear.

The Examiner contends that claims 39-59 are indefinite, because “[c]laim 39 also recites ‘determining an average transformed profile of all transformed experimental profiles

and transformed reference profiles.” The Examiner further contends that “[i]t is not clear whether two average profiles are determined separately for all TA_m or/and all TC_m ; one average profile is determined for all TA_m and TC_m , etc” (Office Action, third paragraph, page 11). Applicant respectfully disagrees.

Step (i) in claim 39 recites “determining **an** average transformed profile of **all** transformed experiment profiles $\{TA_m\}$ **and** transformed reference profiles $\{TC_m\}$ ” (emphasis added). It is clear that there is only **one** overall average profile determined based on **all** experiment profiles $\{TA_m\}$ and reference profiles $\{TC_m\}$. A description of the average profile is found, for example, at page 38, lines 11-15 and page 41, lines 14-19 of the specification. As such, the meaning of the average profile is clear. Therefore, the rejection of claim 39 is obviated. Claims 40-59 depend from claim 39. Therefore, the rejection of claims 39-59 should be withdrawn.

The Examiner contends that claims 40-59 are indefinite, because claim 40 “recites the limitation ‘wherein said difference is determined using a subset . . . in said transformed profiles.’” The Examiner contends that the “antecedent basis of the limitation ‘said transformed profiles’ is not clear because the claim recites $\{TA_m\}$, $\{TC_m\}$, and an **average** transformed profile” (Office Action, fourth paragraph, page 11).

Claim 40 depends from claim 39. The amended claim 39 recites that a first difference is “between each said transformed experiment profile and said average transformed profile” and a second difference is “between each said transformed reference profile and said average transformed profile.” Applicant has accordingly amended claim 40 to be consistent with the language of claim 39. As such, the antecedent basis is clear; and thus the rejection of claim 40 is obviated. Claim 41-59 depend from claim 40. Therefore, the rejection of claims 40-59 should be withdrawn.

The Examiner contends that claims 40-59 are indefinite, because it is further not clear whether “determining” and “using” are intended to be active, positive steps of the method of claim 40 or merely an intended use of the method (Office Action, fourth paragraph, page 11).

Claim 40 has been amended to replace “determined using” with the positive method steps of “calculating.” The amendments have rendered the Examiner’s rejection moot. Thus, the rejection of claim 40 should be withdrawn. Claims 41-59 depend from claim 40. Therefore, the rejection of claims 40-59 should be withdrawn.

The Examiner contends the claims 41-59 are indefinite, because claim 41 recites the limitation “wherein said subset of measurements in the transformed profiles consists of measurements that are ranked similarly between an experiment or reference profiles and said average profile.” Firstly, the Examiner contends that “[i]t is not clear whether the limitation ‘the profiles’ is intended to comprise an average profile, only A_m or C_m , both A_m and C_m , etc.” Secondly, the Examiner contends that “[i]t is not clear what is ranked, *e.g.*, experimental measurements, reference measurements, average measurements, etc., and between what ranked measurements the similarity is assessed.” Thirdly, the Examiner contends that “[i]t is also unclear whether measurements are ranked, for example, in each profile, or measurements are ranked between the value of measurements in a reference profile (*e.g.*, maximum measurement is 10) and the value of measurements in an average profile (*e.g.*, minimum measurement is 5) (*i.e.*, experimental measurements are ranked between 5 and 10).” Lastly, the Examiner contends that it is unclear whether “reference” and “experiment” profiles recited in claim 41 are intended to be “transformed” profiles (Office Action, fifth paragraph, page 11 bridging to first paragraph, page 12).

As to the Examiner’s first contention, Applicant has amended claim 41 to recite “each said first subset consists of transformed measurements that are ranked similarly between each said transformed experiment profile and said average transformed profile” and to recite “each said second subset consists of transformed measurements that are ranked similarly between each said transformed reference profile and said average transformed profile.” The Examiner’s first contention is thus rendered moot in light of the amendment. Therefore, basis for the Examiner’s first contention is obviated.

The amended claim 41 recites “transformed measurements that are ranked similarly between said transformed experiment profile and said average transformed profile” and “transformed measurements that are ranked similarly between each said transformed reference profile and said average transformed profile.” The amended claim 41 clearly recites that transformed measurements are ranked, which thus renders the Examiner’s second contention moot. A detailed description of ranking is found, for example, at page 38, line 8, through page 39, line 9 of the specification. Thus, the rejection of claim 41 based on the second contention is also obviated. As recited in claim 41, the transformed measurements are ranked, for example, between an transformed experiment profile and a transformed average profile according to the ranked order of the transformed measurements, *e.g.*, according the measurement index value k (*e.g.*, index of probes); thereby rendering the Examiner’s third

contention moot. Lastly, it is clear from the express language of the amended claim 41 that the profiles recited in claim 41 are transformed profiles, which renders the Examiner's last contention moot. Accordingly, the rejection of claim 41 should be withdrawn. Claims 42-59 depend from claim 41; and therefore, the rejection of claims 42-59 also should be withdrawn.

The Examiner contends the claims 42-59 are indefinite, because claim 42 recites the limitation "claim 41, wherein said comparing in step (a2) is carried out by a method comprising [steps] (a2i) binning measurements . . . and (div)." The Examiner contends that the limitation "said comparing" does not have an antecedent basis because claim 41 does not recite a step of "comparing." The Examiner also contends that it is further unclear whether each bin comprises only A or C measurements OR both A and C" (Office Action, second paragraph, Page 12). Applicant respectfully disagrees.

Claim 42 has been amended to replace "said comparing" with "said adjusting step (a2)." Claim 42 depends indirectly from claim 39, which recite "(a2) adjusting . . .," thus providing the proper antecedent basis.

Claim 40 recites "a first subset of transformed measurements of said plurality of different cellular constituents between each said transformed experiment profile and said average transformed profile" and "a second subset of transformed measurements of said plurality of different cellular constituents between each said transformed reference profile and said average transformed profile." When a first subset or a second subset are binned into a plurality of bins as in claim 42, each bin will comprise either measurements for a transformed experiment profile and a transformed average profile (in the case of the first subset) *or* measurements for a transformed reference profile and a transformed average profile (in the case of the second subset). As such, claim 42 is clear; thus the rejection of claim 42 should be withdrawn.

Claim 42 depends from claim 30. The Examiner contends that claims 42-59 are indefinite, because it is also unclear whether steps (a2i)-(a2iv) recited in claim 42 are intended to be active, positive steps of the method recited in claim 30 or merely an intended use of the method. The Examiner further contends that if it is the former, then it is not clear where the steps fit within the steps recited in claim 30 and whether the steps (a2i)-(a2iv) are intended to be added to or substitute steps of claim 30 (Office Action, third paragraph, Page 12).

Applicant respectfully point out that claim 42 recites steps (a2i)-(a2iv) that further specify the adjusting step (a2) of claim 39 which in turn further specifies the step of removing nonlinearity of claim 38. Claim 38 specifies that the processing step (a) of claim 30 further comprises removing nonlinearity. Thus, it is clear that steps (a2i)-(a2iv) are affirmative additional steps in the processing step of claims 30. Thus claim 42 is clear, and the rejection of claim 42 should be withdrawn. Claims 43-59 depend from claim 41 and therefore, the rejection of claims 43-59 also should be withdrawn.

The Examiner contends that claims 43-59 are indefinite, because claims 43 and 45 recite “experimental profile A_m ” and “reference profile C_m .” Claims 43 and 45 depend from claim 30, which recites a processed experiment profile identified as A_m and a processed reference profile identified C_m . The Examiner contends that it is not clear what “profiles” are intended in claims 43 and 45 (Office action, first paragraph, Page 13).

Applicant respectfully points out that claim 43 has been amended to recite said “processed” experiment profile A_m and said “processed” reference profile C_m to be consistent with the language of claim 30. Similarly, claim 45 has been amended to recite each “processed” profile pair $\{A_m, C_m\}$, and said “processed” experiment profile A_m , to be consistent with the language of claim 30. Therefore, claims 43 and 45 are clear, and the rejection of claims 43 and 45 should be withdrawn.

Accordingly, Applicant respectfully requests that the 35 U.S.C. § 112 rejection of claims 1-59 and 66 be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 1-18, 25, 30-31, 58-59, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by International Application PCT/US02/20835 to Weng and Dai, filed on July 1, 2002 and published as WO 03/004677 on January 16, 2003 (hereinafter “Weng 2002”).

The Examiner contends that Weng 2002 anticipates claims 1-4 and 66 of the present invention for the following reasons. First, the Examiner contends that Weng 2002 “discloses a method of error correction for a pair of profiles A v. C , wherein A is an experiment profile and comprises data sets $\{A(i)\}$ and C is a reference profile comprising data sets $\{C(i)\}$ (p. 19-28; claims 1-5).” Secondly, the Examiner contends that Weng 2002 “discloses a measured

background noise level of measurement of cellular constituent (i), i.e., $Abkg(i)$, and calculating an average background profile for every $A(i)$ (claims 19-21).” Thirdly, the Examiner contends that Weng 2002 “discloses calculating an average profile (claim 20 and p. 21) and determining a differential profile (claims 1-8 and 19-21; pages 19-28).” Lastly, the Examiner also contends that Weng 2002 “discloses generating an error-adjusted experimental profile using a differential reference profile (claims 1-5 and 19-21; pages 19-28)” (Office Action, fourth paragraph, page 13). Applicant respectfully disagrees.

Weng 2002 discloses a method for generating an error-corrected differential profile $A \text{ v. } B$ where profiles A and B are obtained from different experiments. To achieve this goal, Weng 2002 uses data sets A , B , C_A and C_B . Profiles A and C_A are measured in the same experiment; and profiles B and C_B are measured in the same experiment. The method of Weng 2002 requires differences between C_A and C_B be calculated, which are then used as common systematic cross-experiment errors to correct errors in profiles A and B . By doing so, profiles A and B are adjusted by the same systematic cross-experiment errors, thereby generating a new virtual error-corrected differential profile $A \text{ v. } B$ that is not based on measurement data from the same experiment.

Unlike Weng 2002, Claims 1, 30, and 66 do not generate a new profile pair of measurement data from two different experiments. Instead, claims 1, 30, and 66 are directed to methods that comprise calculating a differential reference profile to correct errors in at least one experiment profile A_m of said plurality of pairs of profiles $\{A_m, C_m\}$. The differential reference profile is calculated based on the differences between a particular reference profile C_m and an average reference profile \overline{C} . The presently claimed invention differs from Weng in at least two aspects. First, the presently claimed invention calculates an average reference profile. Claim 1 of the instant applicant recites “calculating an average reference profile \overline{C} of said plurality of reference profiles $\{C_m\}$, where $m = 1, 2, \dots, M$.” The average reference profile as claimed comprises a data set $\{\overline{C}(k)\}$ that contains averaged measurements or averaged transformed measurements of a plurality of cellular constituents. Claims 30 and 66 recite similar limitations to the foregoing recitation of claim 1. Weng does *not* disclose such an average profile. Weng 2002 discloses calculating *mean background noise levels* that are specific for a particular experiment. For example, claim 20 of Weng expressly recites two equations for calculating average background profiles for a first experiment condition (e.g., A) and a second experiment condition (e.g., B). Weng 2002, as

cited by the Examiner, discloses calculating mean background noise levels

$$Abkg = \frac{1}{N} \sum_{i=1}^N Abkg(i) \text{ and } Bbkg = \frac{1}{N} \sum_{i=1}^N Bbkg(i) \text{ for data sets A and B, where mean}$$

background noise levels (*e.g.*, *Abkg* and *Bbkg*) are mean values that may be used to offset background noise among measurement. As illustrated by the above equations of claim 19-21 and on page 21 of Weng 2002, the mean background noise level of Weng 2002 is **only** a mean value **not** an average profile. Therefore, the Examiner's second contention is erroneous. Second, claim 1 also recites "determining, for at least one profile pair $\{A_m, C_m\}$ where $m \in \{1, 2, \dots, M\}$ of said plurality of pairs of profiles $\{A_m, C_m\}$, a differential reference profile computed between C_m and \bar{C} ." Claims 30 and 66 have similar recitations. Weng 2002 does **not** disclose a differential reference profile as recited in claims 1, 30, and 66 since Weng 2002 does not use an average profile as recited in the claims. As such, Weng 2002 does not disclose all the elements of claims 1, 30, and 66 of the instant application and thus does not anticipate these claims. The remaining claims either depend from or incorporate all the limitations of claims 1, 30, and 66, and thus also are not anticipated.

Accordingly, Applicant respectfully requests that the 35 U.S.C. § 102 rejection of claims 1-18, 25, 30, 31, 58, 59 and 66 be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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Adriane M. Antler 32,605
Adriane M. Antler (Reg. No.)
JONES DAY
222 East 41st Street
New York, New York 10017-6702
Phone: (212) 326-3939
by: Musa Abraham
10012